

A Network Analysis of Synthetic-Lethal Genetic Interaction

Wong, Sharyl L.¹, Zhang, Lan V.¹, Berriz, Gabriel¹, Goldberg, Debra S.¹, King, Oliver D.¹, Tong, Amy H.Y.², Li, Zhijian², Lesage, Guillaume³, Vidal, Marc⁴, Andrews, Brenda², Bussey, Howard³, Boone, Charles², Roth, Frederick P.^{*1}

¹*Department of Biological Chemistry and Molecular Pharmacology, Harvard Medical School, Boston, MA, USA;* ²*Banting and Best Department of Medical Research and Department of Medical Genetics and Microbiology, University of Toronto, Toronto, Ontario, Canada;* ³*Department of Biology, McGill University, Montreal, Quebec, Canada;* ⁴*Department of Cancer Biology, Dana-Farber Cancer Institute and Department of Genetics, Harvard Medical School, Boston, MA, USA*

Two genes have a synthetic lethal interaction if the combination of two mutations, neither by itself lethal, causes cell death. Such an interaction represents genetic buffering of one gene by another, and contributes to the robustness of an organism to mutation. There are many other ways to describe the relationship between two genes or proteins. We assembled a diverse collection of gene-gene and protein-protein relationships in *S. cerevisiae*, including: homology, correlated expression, co-localization, common transcriptional regulation, chromosomal proximity, similarity in phylogenetic profile, and physical interaction. We then examined synthetic interactions from the systematic genetic analysis (SGA) of ~500,000 gene pairs. Here we characterize relationships between the network of synthetic genetic interactions and other biological networks. Our analysis clearly demonstrates the value of SGA in characterizing gene function. Furthermore, we have exploited discovered relationships to predict synthetic genetic interactions, with potential relevance to multigenic human disease.

O.D.K. was supported by an NRSA Fellowship from the NIH/NHGRI. D.S.G. was supported by an NSF Postdoctoral Research Fellowship in Interdisciplinary Informatics. F.P.R. was supported in part by an NIH/NCI National Programs of Excellence in Biomedical Computing Planning Grant.